IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: L. TSOREF, et al.

Serial Number: 10/042,735

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For: BONE AGE ASSESSMENT USING ULTRASOUND

Examiner: JAWORSKI, FRANCIS J

Art Unit: 3768

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

APPEAL BRIEF

Sir:

Further to a Notification of Non-Compliant Appeal Brief dated December 1, 2006, the attached Transmittal Letter has been revised to correct an obvious error in the title of the invention. Following is applicants brief on appeal as filed on September 14, 2006.

(c1)(i) Real Party of Interest:

The real party of interest in the present application is: Beam-Med Ltd.

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(c1)(ii) Related Appeals and Interferences:

None

(c1)(iii) Status of claims:

Claims 1-63, of which claims 1, 49, 62 and 63 are independent claims, are pending. All the claims stand rejected and all are appealed.

(c1)(iv) Status of Amendments:

There are no current outstanding amendments

(c1)(v) Summary of Claimed Subject Matter

In the summary below limitations of the independent claims are shown in italicized script and references to the limitations in the specification and figures are given in square brackets in plain script

Independent claim 1 claims an ultrasound method of assessing bone age. The method comprises:

transmitting acoustic energy into an ossification actuated skeletal structure of the body of a subject so that the acoustic energy propagates substantially transverse to the structure;

[An ossification actuated skeletal structure comprises an ossification center which may be a primary or secondary ossification center. A primary ossification center begins from a central portion of a bone and progresses toward the periphery. (page 8 lines 30, 31). In Fig. 1 primary ossification centers are generally indicated by shaded areas (*e.g.* Fig. 1 106a, 104a, 112a). Some bones have additional secondary ossification centers that appear as a strip of cartilage between ossified bone sections, for example region cartilaginous growth plate 242 that is situated between an epiphysis 232b and a metaphysis 232a, in Fig. 1A (page 9 lines 3-5).]

so that the acoustic energy propagates substantially transverse to the structure;

[Fig. 1 shows a transmitter 120 that transmits ultrasound along a region 276 which has a direction transverse to an ossification activated skeletal structure, which is a region of the wrist (page 9 lines 14-19). Fig 2A schematically shows transducers 256 and 258 transmitting ultrasound through ossification centers of the wrist and a finger in directions transverse to the wrist and the finger.]

receiving an acoustic signal from said ossification-actuated skeletal structure responsive to said transmitted acoustic energy;

[Acoustic receiver 122 (Fig. 1 and page 9 line 14-20) and acoustic receiver 258 (Fig. 2A, and page 17 lines 16-22) receive acoustic signal responsive to acoustic energy transmitted to propagate transversely through ossification actuated skeletal structures.]

analyzing the acoustic signal to determine at least one effect of said structure on said signal

[Graph 260 in Fig. 2B shows acoustic signals received by receiver 258 that are analyzed to determine effect of the structure on speed of sound and the specification (page 17 line 20 to page 18 line 7) discusses the signals. Other effects of the structure on the acoustic signals are dispersion (page 10, lines 22-27) and attenuation (page 10 lines 28-33)]

and estimating the age of the structure from said determined effect.

[The values shown in graph 260 are used to estimate bone age (page 18 line 11-30); discussion from page 9 line 26 - page 14 line 10]

Independent claim 49 is an apparatus claim that claims apparatus for estimating bone age. The apparatus comprises:

an acoustic transmitter and an acoustic receiver positioned facing each other so that an ossification-actuated skeletal structure may be positioned between them;

[Receiver 122 and transmitter 120 (Fig. 1 and page 9 line 14-23), and ultrasound transmitter 256 and ultrasound receiver 258 (Fig. 2A and page 17 line 16-page 18 line 7)]

an electronic moveable gantry that adjusts the position of said acoustic transmitter and said acoustic receiver in relation to said ossification-actuated structure;

[Gantry 174 (Fig. 1 and page 9 line 15, page 15 lines 23-page 16 line 2); gantry 274 (Fig. 2A, and page 20 line 13-18)]

a computer system

[Computer system 142 (Figs. 1 and 2A, and page 9 lines 24-26, page 10 line 16-21, page 16 line 21, page 20 line 14-18, line 330]

that performs one or more functions of:

positioning of said moveable gantry;

[Computer system 142, (page 16 lines 20-22, page 20 lines 14-16)]

controlling acoustic signals transmitted by said acoustic transmitter;

[Computer system 142, (page 9 lines 24-26, page 20 lines 14-16)]

receiving acoustic signals from said receiver responsive to said transmitted signals;

[Computer system 142, (page 10 lines 16-21, page 20 lines 32-33)]

and

estimating said bone age responsive to said received signals.

[Computer system 142, (page 9 line 24, page 10 lines 16-21) and discussion from page 10 line 22 - page 14 line 10 and discussion of signal processing to determine age from page 20 lines 14-18, page 20 lines 32-33)]

Also note page 6 line 27-page 7 line 5.

Independent claim 62 claims a method of measuring bone age. The method comprises:

transmitting acoustic energy into a region of the body of a subject at which cartilage of a skeletal structure is undergoing ossification or at which cartilage of a skeletal structure that has completed growth was last to ossify so that the acoustic energy propagates substantially transverse to the structure;

[Page 2 line 24-29, page 3 line 1, page 9 lines 3-10 and Figs. 1, 2. Figs. 1 and 2 show transmitting ultrasound to propagate transversally through skeletal structure in regions of cartilage and regions where skeletal structure is last to ossify *e.g.* growth plate 242 (page 9 line 8 and shown in Figs. 1 and 2)].

receiving an acoustic signal from the skeletal structure responsive to said transmitted acoustic energy;

[Acoustic receiver 122 (Fig. 1 and page 9 line 14-20) and acoustic receiver 258 (Fig. 2A, and page 17 lines 16-22) receive acoustic signal responsive to acoustic energy transmitted to propagate transversely through ossification actuated skeletal structures.] *analyzing the acoustic signal to determine at least one effect of said structure on said signal;*

[Graph 260 in Fig. 2B shows acoustic signals received by receiver 258 that are analyzed to determine effect of the structure on speed of sound and the specification (page 17 line 20 to page 18 line 7) discusses the signals. Other effects of the structure on the acoustic signals are dispersion (page 10, lines 22-27) and attenuation (page 10 lines 28-33)]

and estimating the age of the structure from said determined effect.

[The values shown in graph 260 in Fig. 2B are used to estimate bone age (page 18 line 11-30); discussion from page 9 line 26 - page 14 line 10]

Independent claim 63 claims a method of determining bone age. The method comprises:

measuring a first acoustic velocity through a bone in a direction transverse to the bone;

measuring a second acoustic velocity along a length of the bone;

determining a ratio between the first and second acoustic velocities; and

using the ratio to determine bone age.

[Page 18 lines 21-26]

(c1)(vi) Grounds of Rejection to be Reviewed on Appeal

(vi.1) Rejection of claims 1-40, 46, and 62 under 35 U.S.C. §103(a) as being unpatentable over US 6,468,215 to Sarvazyan et al in view of US 5,483,965 to Wiener et al.

(vi.2) Rejection of claims 1-25, 27-29, 36-38, 40- 48, and 62 as being unpatentable under 35 U.S.C. §103(a) over Sarvazyan in view of Wiener and US 5,895,364 to Donskoy, (claims 41-45, 47 and 48 are rejected further in view of applicants specification);

(vi.3) Rejection of claims 1-25, 27-29, 36-38, 40-48, 59- 62 as being unpatentable under 35 U.S.C. §103(a) over Sarvazyan in view of Wiener and US 5,806,520 to Berger et al, (claims 41-45, 47-48, 59-61 are rejected further in view of applicants specification);

(vi.4) Rejection of claims 49-57 as being unpatentable over Sarvazyan and Wiener, further in view of Berger;

(vi.5) Rejection of claim 63 as being unpatentable under U.S.C. §103(a) over Sarvazyan and Wiener further in view of US 5,197, 475 to Antich et al.

(vi.6) Rejection of claim 58 as being unpatentable under U.S.C. §103(a) over Sarvazyan and Wiener further in view of Berger and further in view of Kaufman et al.

(c1)(vii) Arguments

General comment regarding the Examiner's failure to support a prima facie case for obviousness because in accordance with MPEP 2145 X. D. 2 "References Cannot be Combined Where References Teach Away from Their Combination"

All of the claims stand rejected based on obviousness over Sarvazyan in view of Wiener, alone or combined with other references. Claim 1 states that the acoustic waves are propagated substantially traverse to the structure. Claims 62 and 63 have substantially the same limitation. Claim 49 provides that two transducers are placed on opposite sides of a bone, which implies the same thing. All of the claims require estimating bone age from measurements of the transversely propagated waves.

Sarvazyan, which does teach bone age determination, not only does not teach transverse propagation, it actually makes a number of statements that teach against such propagation. The

Examiner appears to be confusing the direction of propagation of acoustic waves (which is what is claimed in claims 1 and 62) with the direction of stress in the bone that accompanies such waves. Applicants submit that this is a fatal flaw in the Examiner's reasoning and is similar to confusing the direction of the fields in an electromagnetic wave with the direction of propagation of the waves.

Furthermore while Weiner does use transverse propagation for measurement of osteoporosis, Sarvazyan specifically states that these should not be used for measurement of bone age.

Thus, the rejections are based on an improper, combining of references which the Examiner insists on promoting where one reference clearly states that the technique of a second reference is unsuitable for a particular measurement. The contention of impropriety of the combination is supported by MPEP 2145 X. D. 2 which states:

"It is improper to combine references where references teach away from their combination. *In re* Grasselli, 713 F.2D 731, 743, 218 USPQ 769, 779 (Fed Cir. 1983) (The claimed catalyst which contained both iron and an alkali metal was not suggested by the combination of a reference which taught the interchangeability of antimony and alkali metal with the same beneficial result, combined with a reference expressly excluding antimony from and adding iron to, a catalyst.)."

The arguments are developed and detailed with respect to each ground of rejection below.

Argument with respect to (vi.1): Rejection of claims 1-40, 46, and 62 under 35 U.S.C. §103(a) as being unpatentable over US 6,468,215 to Sarvazyan et al in view of US 5,483,965 to Wiener et al.

The Examiner promulgates a first argument for combining Sarvazyan and Wiener and that the combination teaches determining bone age using "transverse" measurements because: "Sarvazyan et al uses both longitudinal and flexural components of bone measurements to assess skeletal age. Since Wiener et al in Fig. 6 note that both velocity and attenuation measurements for cortical bone may be made using a single transducer and reflective member … it would have been obvious to effect Sarvazyan et al expedient to obtain cortical flexural velocity and attenuation in this fashion."

The Examiner's argument appears to be a syllogism of the following form:

1. Sarvazyan teaches determining bone age using "longitudinal and flexural components of bone measurements to assess skeletal age".

2. Wiener teaches measuring velocity and attenuation for cortical bone (Fig. 6) using a single reflective member (as a result of which Wiener performs measurements by propagating sound transverse to bone).

3. Therefore, it is obvious to provide the flexural measurements used by Sarvazyan to determine age of a bone using the method of Wiener which method involves measuring velocity of sound propagated transverse to the bone; ergo Sarvazyan and Wiener provide the invention of independent claims 1 and 62.

Applicants do not understand what "longitudinal and flexural components of bone measurements" as used by the Examiner means, but agrees that Sarvazyan uses characteristics, such as velocity, attenuation etc. of *longitudinal and flexural waves* as explicitly noted for example on column 3 lines 10. Applicants further agree that Wiener teaches performing measurements of ultrasound transmitted into and transverse to the bone. However, Sarvazyan explicitly and repeatedly limits his measurement to measurements of ultrasound propagated over trajectories *along a bone* and in particular a surface of a bone and not transverse to the bone.

For example, in Sarvazyan's abstract the invention is described as "A method of assessment of bone conditions comprises acquiring unilateral ultrasonic measurements along *the trajectory over the surface of an examined bone*."

The apparatus for practicing Sarvazyan's invention, as shown for example in Figs. 2 and 5 and discussed in descriptions of the figures, is configured only for acquiring measurements of sound transmitted in bone along a trajectory not transverse to the bone but along a surface of the bone. For example, as noted with respect to Fig. 2 (column 4, lines 53-55), "*One of transducers 22 is an emitter and a second one of transducers 22 is a receiver of ultrasonic waves propagated along bone 14*. The transducers are located on a same side of the bone and are shown propagating a sound wave (indicated by a dashed line) along the bone from one to the other and not transverse to the bone.

However, not only does Sarvazyan teach ultrasound trajectories only along a bone and not transverse to the bone but in fact teaches away from transverse bone measurements indicated and taught by Wiener. The only example of transverse measurements detailed by Wiener, comprises measurements transverse to the heel. With regard to such measurements and techniques, Sarvazyan notes "There is a numerical superiority of heel QUS techniques over long

bone QUS allowing good opportunity to evaluate density of *trabecular structure* in osteoporosis, but limiting QUS application for other sites of the skeleton, *thereby hampering* comprehensive evaluation of osteoporosis and *monitoring of bone growth and ossification during childhood*." (column 2 lines 46-52, italics added.) The preceding quote from Sarvazyan, indicates that while heel QUS techniques, such as the Wiener techniques, provide information regarding *trabecular bone, they are not suitable for "monitoring of bone growth and ossification during childhood"*. Sarvazyan therefore explicitly teaches away from and discourages combining any of the methods of Wiener with those of Sarvazyan.

In view of the above and the noted explicit teaching away by Sarvazyan, Sarvazyan and Wiener cannot be combined to provide the inventions of any of the independent claims (and claims dependent on them) since in accordance with MPEP 2145 X. D. 2, "References Cannot be Combined Where References Teach Away from Their Combination". The conclusion of the "Examiner's" syllogism is therefore not tenable and applicants submit that the Examiner has thus not established a *prima facie* case of obviousness.

However, the syllogism is untenable not only because its conclusion flies in the face of the teaching of Sarvazyan and MPEP 2145 X. D. 2, but also because statements in the syllogism are not supported.

For example, the Examiner submits in his argument, and as noted in step 2 of the syllogism, that Wiener teaches measuring *cortical bone* and draws the applicants attention to Fig. 6. The reference to cortical bone is required because Sarvazyan implicitly and explicitly teaches that his measurements are performed on cortical bone. (note column 3 lines 21-25, column 7 lines 35-37 and that the Sarvazyan measurements are consistently described as being preformed on the surface of long bones, which is cortical bone, see for example, column 3 line 44 and Fig. 1 and description thereof).

However, despite the Examiner's assertion, Wiener never mentions cortical bone, but instead describes his measurements as suitable measuring "quality of cancellous bone matrix" (column 9 lines 14-16) or of the "os calcis as measured through the heel of a human patient" (column 12 lines 56-62). With respect to Wiener's Fig. 6, the figure shows transverse acoustic measurements being made on an object referenced by the number "32" "placed between the two transducers 21 so that acoustic signals may be transmitted through the object. This object 32 represents a member, such as a bone, or some material with known acoustic properties such as distilled water or a neoprene reference block." The object is not described as cortical bone.

Furthermore, the Examiner bases his conclusion, as noted in step 3 of the syllogism, that it is obvious to use Wiener to provide Sarvazyan's measurements because it is obvious to use Wiener for performing flexural measurements. However, whereas Sarvazyan explains how to distinguish longitudinal waves from flexural waves and to determine and use their respective characteristics independent of each other (*e.g.* Fig. 7 and discussion thereof) Wiener never mentions flexural waves or their equivalent in any manner. Again only reference to the present invention endows Wiener with flexural waves.

The Examiner promulgates a second alternative argument for combining Sarvazyan and Wiener because "since Sarvazyan et al suggest using attenuation and velocity to assess gestational and/or developmental ages of bone it would have been obvious to extend the Wiener et al pathology applicability to skeletal age (deficiency) measurement."

Applicants traverse the Examiner's second alternative argument for the same reasons that the Examiner's first argument is traversed and in addition because in transverse measurements, such as those described in Wiener, sound waves travel not only through cortical bone but generally also through *trabecular* bone. As a result, transverse measurements provide information *different from that of measurements along bone* and neither the Examiner nor any of the cited references explain how the different information provided by Wiener synergizes in any way to support combining Wiener and Sarvazyan. Therefore, it is decidedly *not obvious* to perform the cortical velocity and/or attenuation measurements of Sarvazyan in the transverse fashion of Wiener.

In view of the above, applicants submit that the Examiner's second alternative argument does not establish a prima facie obvious rejection of claim and that the claims are improperly rejected.

Argument with respect to (vi.2): Rejection of claims 1-25, 27-29, 36-38, 40-48, and 62 as being unpatentable under 35 U.S.C. §103(a) over Sarvazyan in view of Wiener and US 5,895,364 to Donskoy;

Applicants submit that firstly, this rejection is improper for not providing a *prima facie* case for combining the Wiener and Sarvazyan references, for the reasons given above.

With respect to rejection (vi.2) the Examiner cites Donskoy in addition to Wiener and Sarvazyan for Donskoy's "col. 1 teaching that flexural measurements mean across or transverse to bone and longitudinal means along bone. Hence Sarvazyan et al are referring to across as well

as along bone and are compositing the two types of measurements in their analysis by virtue of this art supplied definition."

In addition, with respect to the specific arguments provided by the Examiner in regard to Donsky, applicants note that the words "flexural" and "longitudinal" are recited in only three places in column 1 of Donskoy. In none of the recitations is a flexural measurement defined as meaning "across" or "transverse" to bone or a longitudinal measurement as meaning "along" bone. Applicants submit that the fact that a wave is flexural does not at all describe the direction of the wave, but only that the wave involves shear.

Applicants have also searched the remainder of Donskoy for the definitions noted by the Examiner, but has failed to locate such definitions. The three relevant recitations in column 1 are quoted below.

1) "Subsonic techniques for determining the in vivo properties of bone, known as impedance and resonance methods are based on measurement of the response of a bone to a flexural wave excitation in the frequency range 200 to 1000 Hz." (column 1 lines 32-36)

2) "Interpretation of subsonic measurement of flexural vibration of bone is also a difficult task and to a great extent, depends upon a corresponding mathematical model of the test object." (column 1 lines 47-50)

3) "A non-invasive, nonhazardous and cost effective infrasound resonance method for the quantitative measurement and monitoring of bone quality has now been developed involving the measurement of the rigid body longitudinal resonance of a bone." (column 1 lines 53-57)

In view of the above, applicants submit that the Examiner's contention is not supported by Donskoy and that the rejections based on Donskoy are not valid. Donskey cannot under any circumstances contribute to overcome the deficiencies of Wiener and Sarvazyan or to make the "combination" any more valid.

Applicants note that the above remarks with respect to the definitions purportedly provided by Donskoy were brought to the Examiner's attention verbatim in the applicants response filed May 19, 2005 and in the applicants response filed on September 7, 2004, the applicants noted that the definitions credited to Donskoy could not be found in column 1. None of the applicants remarks with respect to Donskoy were addressed by the Examiner as required by MPEP 707.07(f) and Examiner Note 7.37.

Argument with respect to (vi.3): Rejection of claims 1-25, 27-29, 36-38, 40-48, 59-62 as being unpatentable under 35 U.S.C. §103(a) over Sarvazyan in view of Wiener and US 5,806,520 to Berger et al; and (vi.6) Rejection of claim 58 as being unpatentable under U.S.C. §103(a) over Sarvazyan and Wiener further in view of Berger and further in view of Kaufman et al.

Applicants first submit that this rejection is, as is each of the other rejections discussed above, improper for not providing a *prima facie* case for combining the Wiener and Sarvazyan references, for the reasons given above.

In rejection (vi.3), the Examiner provides a further alternative argument for rejection claims 1-25, 27-29, 36-38, 40-48, 59-62 by citing Berger in addition to Wiener and Sarvazyn. Berger is cited because "Berger is directed to measurement of skeletal maturation in neonates using transverse through-transmission with opposed transducer faces, see col. 2 lines 11- 22, whereupon it would have been obvious to adapt same for long bone scanning in Sarvazyan in order to accurately known the exact path distance which the ultrasound takes via this caliper style transducer separation setting."

Applicants submit that the Berger reference is cumulative compared to Weiner since the Examiner is using Berger to prove exactly the same thing as Weiner based on a substantially similar disclosure. Wiener describes and shows opposed transducer faces that provide a "caliper effect" (see Fig 4 and description thereof) for acquiring transverse acoustic measurements. As a result Berger, for the purpose of providing a caliper effect stated by the Examiner, appears to be cumulative to Wiener and would not be combinable with Sarvazyan, for the same reason given above for the combination of Sarvazyan with Weiner.

Be that as it may, applicants reject combining transverse measurements with Sarvazyan and in particular the combination of Sarvazyan and/or Wiener's and/or Berger's transverse measurements for the same reasons as noted above with respect to rejection (vi.1) . Furthermore, since Sarvazyan performs measurements for acoustic trajectories along bone and Berger provides measurements for acoustic trajectories transverse to bone applicants submit that Berger's method for defining path lengths are not relevant to those of Sarvazyan. In addition, applicants note that Sarvazyan (column 4 lines 55-61) does not appear to have a problem defining exact ultrasound path distances for ultrasound transmitted along bone as the following quote (column 4 lines 55-61) attests. "Transducers 22 are fixed on a rigid frame 24 to provide a constant base for measurements of ultrasound propagation parameters in the pulse transmission

mode. Base length L is chosen on the basis of a trade off between reliable detection of ultrasound propagation velocities of longitudinal and flexural wave components and spatial resolution profiles 15."

As noted above Berger appears cumulative but if a rationale for adding Berger is that Berger recites using their methods for skeletal maturation in neonates, applicants note that Berger recites maturation not in the context of bone age, but in the context of a "degree of mineralization of the skeleton in particular in order to follow the evolution of the bone architecture or of the elasticity of the bone structure" (column 9 line 59-64). It is noted that a neonate is a newborn up to the age of 4 weeks. None of the cited documents provide motivation or indicate how to extrapolate a method specifically limited to measuring degree bone mineralization of a newborn over a period of 4 weeks to a method of determining bone age.

In view of the above applicants submit that there is no motivation to combine Berger with Sarvazyan and Wiener on the basis of the caliper effect or a teaching as to how to combine Berger with Sarvazyan and Wiener on the basis of neophyte skeletal mineralization. Applicants therefore contend that the Examiner has not established a prima facie case for obviousness and claims 1-25, 27-29, 36-38, 40, 46, and 62 are patentable over the combination of references.

Argument with respect to (vi.4): Rejection of claims 49-57 as being unpatentable over Sarvazyan and Wiener, further in view of Berger;

Applicants first submit that this rejection is, as is each of the other rejections discussed above, improper for not providing a *prima facie* case for combining the Wiener and Sarvazyan references, for the reasons given above.

In rejection (vi.4) apparatus claims 49-57 are rejected over Sarvazyan and/or Wiener and further in view of Berger. The Examiner argues that it would have been obvious to use Berger "as an extension of bone integrity and/or density ultrasound measurement by using facing transducer pairs since this allows callipering of the distance of the acoustic transmission path over which the measurement is conducted."

Claim 49 is the only independent claim in the group of claims 49-57. The claim recites an acoustic transmitter and an acoustic receiver facing each other for acquiring transverse bone measurements and a computer system that receives signal generated by the receiver responsive to ultrasound propagating transverse to a bone structure and uses the signals to estimate the bone age.

Applicants note that none of the cited references comprises or teaches a computer system that processes transverse acoustic signals to determine bone age. Applicants also submit that the computer system recited in claim 49 cannot be forthcoming from a combination of the cited references because the references are not combinable for the same reasons as stated in argument 8.3. Therefore claim 49 and claims dependent thereon are patentable over the references.

Argument with respect to (vi.5): Rejection of claim 63 as being unpatentable under U.S.C. §103(a) over Sarvazyan and Wiener further in view of US 5,197, 475 to Antich et al.

Applicants first submit that this rejection is, as is each of the other rejections discussed above, improper for not providing a *prima facie* case for combining the Wiener and Sarvazyan references, for the reasons given above.

Independent claim 63 claims a method of determining bone age comprising: measuring a first acoustic velocity through a bone in a direction transverse to the bone; measuring a second acoustic velocity along a length of the bone; determining a ratio between the first and second acoustic velocities; and using the ratio to determine bone age.

The claim is rejected as obvious over Sarvazyan and Wiener in view of Antich because it would have been obvious in view of Antich et al "to form ratios of through-bone velocities in order to characterize a bone integrity, understood by Berger et al to include skeletal maturing akin to parameters such as assessed in Antich et al". Applicants respectfully traverse.

The combination of Sarvazyan and Wiener and/or Berger is traversed as above. With respect to Antich, the patent mentions a ratio between velocities in only two places (column 14 lines 23-24 and column 14 lines 49-52). The ratios refer to ratios between results of measurements of velocity using different techniques, a reflection technique and a transmission technique, and are used to compare the measurements and determine a degree to which they are correlated.

In column 14 lines 23-24 the ratio refer to measurements carried out on "laboratory materials which were believed to be essentially isotropic and homogeneous (column 13 lines 22-24). The measurements on the laboratory materials certainly do not apply in any way to claim 63.

In column 14 lines 49-52 the ratio refers to measurements carried out on cortical bone specimens having machined and lapped surfaces (column 13 lines 42-50). A difference of the ratio from 1 is ascribed to the measurements of transmission and reflection velocities being

acquired at different frequencies and additionally because of "material heterogeneities structural geometry and density variations" (column 14 lines 47-61). There is no attempt in the patent to correlate the ratio with age or intimate such a correlation. Indeed, there does not seem to be any indication that the ratio is useable for anything other than to show that the measurements correlate with each other. Applicants therefore submit that the Examiner has not shown how to combine Antich et al with the other references mentioned in the rejection to provide the invention of claim 63 nor provided any motivation to do so and that therefore the reference is not useable to support a prima facie obviousness rejection of the claim.

In view of the above applicants submit that all the claims argued are patentable over the art cited by the Examiner and claims dependent on any of the argued claims are patentable at least through their dependence. Applicants respectfully request that the Board reverse the ruling of the Examiner and allow all the claims.

January 2, 2007

Respectfully submitted,

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(c)(1) (viii) Appendix - Claims under Appeal

1. A method for measuring bone age comprising:

transmitting acoustic energy into an ossification actuated skeletal structure of the body of a subject so that the acoustic energy propagates substantially transverse to the structure;

receiving an acoustic signal from said ossification-actuated skeletal structure responsive to said transmitted acoustic energy;

analyzing the acoustic signal to determine at least one effect of said structure on said signal; and

estimating the age of the structure from said determined effect.

2. A method according to claim 1 wherein said ossification-actuated skeletal structure comprises one or more areas undergoing ossification.

3. A method according to claim 1 wherein said ossification-actuated skeletal structure comprises one or more bones.

4. A method according to claim 1 wherein said ossification-actuated skeletal structure comprises one or more regions of cartilage.

5. A method according to claim 1 wherein said ossification-actuated skeletal structure comprises one or more regions of non-cartilage soft tissue.

6. A method according to claim 5 wherein said ossification-actuated skeletal structure comprises one or more regions of fibrocartilage.

7. A method according to claim 1 wherein said ossification-actuated skeletal structure comprises a region with one or more primary ossification centers.

8. The method according to claim 7 wherein said ossification-actuated skeletal structure comprises one or more of: the bones of the wrist, the bones of the palm, the bones of the tarsus, the mandible.

9. A method according to claim 1 wherein said ossification-actuated skeletal structure comprises a region with one or more secondary ossification centers.

10. The method of claim 9 wherein said ossification-actuated skeletal structure comprises an epiphysis.

11. The method of claim 9 wherein said ossification-actuated skeletal structure comprises a region of one or more of: an ulna, a radius, a femur, a bone of a ray of an extremity.

12. A method according to claim 1 wherein said receiving comprises utilizing two or more different acoustic signals to provide a measure of bone age.

13. A method according to claim 12 wherein said two or more acoustic signals are associated with a same bone.

14. A method according to claim 12 wherein said skeletal structure comprises a portion of each of a plurality of bones and said two or more acoustic signals are associated with paths in different bones.

15. A method according to claim 12 wherein said two or more acoustic signals are received from the same direction.

16. A method according to claim 12 wherein said two or more acoustic signals are received from the different directions.

17. A method according to claim 12 wherein said signal passes through said ossification-actuated skeletal structure.

18. A method according to claim 1 wherein said signal echoes from said one or more structures including an ossification-actuated skeletal structure.

19. A method according to claim 1 wherein said analysis of said signal is responsive to speed of sound from said ossification-actuated skeletal structure.

20. A method according to claim 1 wherein said analysis of said signal is responsive to broadband ultrasound attenuation from said ossification-actuated skeletal structure.

21. A method according to claim 1 wherein said analysis of said signal is responsive to dispersion of ultrasound from said ossification-actuated skeletal structure.

22. A method according to claim 1 wherein said analysis of said signal is performed, at least in part, in the frequency domain.

23. A method according to claim 1 wherein said analysis of said signal is performed, at least in part, in the time domain.

24. A method according to claim 1 wherein said analysis of said signal is responsive to attenuation of an ultrasound signal in said ossification-actuated skeletal structure.

25. A method according to claim 1 wherein said analysis is used to predict adult stature.

26. A method according to claim 1 wherein, to provide an estimate of bone age, said analysis is compared to a database having correlation with one or more of: conventional radiographs, CT images, MRI images and Nuclear Medicine scans.

27. A method according to claim 1 wherein said receiving is from a scanning acoustic signal transmitter.

28. A method according to claim 1 wherein said receiving is from a multi-beam acoustic signal transmitter.

29. A method according to claim 1 wherein said receiving provides two or more acoustic signal measures along an axis of said ossification-actuated skeletal structure.

30. A method according to claim 1 wherein said receiving provides two or more acoustic signal measures radially around said ossification-actuated skeletal structure.

31. A method according to claim 1 wherein said analysis is correlated with a known bone age measurement system.

32. A method according to claim 1 wherein said analysis is responsive to a formula providing a correlation with a known bone age measurement system.

33. A method according to claim 32 wherein said formula is responsive to at least one of speed of sound, broadband ultrasound attenuation, scattering and dispersion of acoustic signal through or from said ossification activated skeletal structure.

34. A method according to claim 32 wherein an estimate of bone age is responsive to time of flight of an acoustic signal between two transducers, with said ossification activated skeletal structure being situated intermediate to said transducers.

35. A method according to claim 26 wherein separate formulas are used to correlate known bone age data with acoustic signals from males and females.

36. A method according to claim 1 wherein said acoustic information is constructed into a database of bone age measurements.

37. A method according to claim 36 wherein said database is arranged according to one or more of: sex, ethnic group, geographic location, nutrition and general inheritance.

38. A method according to claim 36 wherein said database includes two or more measurements of one or more of said ossification-actuated skeletal structure.

39. A method according to claim 36 wherein said database includes one or more measurements of two or more growth stages from said ossification-actuated skeletal structure.

40. A method according to claim 36 wherein said database includes one or more measurements of said ossification-actuated skeletal structure in two or more populations.

41. A method according to claim 36 wherein said received signals are compared to similar signals in a database to predict one or more of adult bone length, density, thickness and resilience and adult stature.

42. A method according to claim 36 wherein said received signals are compared to similar signals in a database to indicate a bone-growth related disorder.

43. A method according to claim 36 wherein said received signals are compared to similar signals in a database to track the progress of a bone-growth related disorder.

44. A method according to claim 36 wherein said received signals are compared to similar signals in a database to track hormone therapy in a growth stature disorder.

45. A method according to claim 36 wherein said received signals are compared to similar signals in a database to indicate one or more growth-plate related disease states, including osteogenic sarcoma, slipped growth plate, premature arrest of growth plate growth and inflammation of growth plate.

46. A method according to claim 36 wherein two or more acoustic measurements are made on a single subject and entered into said database.

47. A method according to claim 36 wherein said two or more acoustic measurements are compared to track one or more growth-related disorders, including precocious puberty, delayed puberty, rickets, kwashiorkor, hypoparathyroidism, pituitary dwarfism and diabetes.

48. A method according to claim 36 wherein said two or more acoustic measurements are compared to track treatment of one or more growth-related disorders, including precocious

puberty, delayed puberty, rickets, kwashiorkor, hypoparathyroidism, pituitary dwarfism and diabetes.

49. An apparatus for estimating bone age comprising:

an acoustic transmitter and an acoustic receiver positioned facing each other so that an ossification-actuated skeletal structure may be positioned between them;

an electronic moveable gantry that adjusts the position of said acoustic transmitter and said acoustic receiver in relation to said ossification-actuated structure;

a computer system that performs one or more functions of:

positioning of said moveable gantry;

controlling acoustic signals transmitted by said acoustic transmitter;

receiving acoustic signals from said receiver responsive to said transmitted signals; and

estimating said bone age responsive to said received signals.

50. The apparatus of claim 49 wherein said apparatus transmits and receives one or more acoustic signals linearly along an axis through said ossification-actuated structure.

51. The apparatus of claim 49 wherein said apparatus transmits and receives one or more acoustic signals radially around an axis through said ossification-actuated structure.

52. The apparatus of claim 49 wherein said computer system controls said acoustic signal transmitter to provide an acoustic signal appropriate for said ossification-actuated structure.

53. The apparatus of claim 49 wherein said computer system estimates said bone age responsive to one of more of: broadband ultrasound attenuation, acoustic backscatter, dispersion of acoustic signal and speed of sound in said ossification-actuated structure.

54. The apparatus of claim 49 wherein said computer system uses an imager to control the position of said acoustic signal receiver and said acoustic signal transmitter.

55. The apparatus of claim 49 said computer system contains a visual display to provide information on said bone age.

56. The apparatus of claim 55 wherein said visual display comprises a graph.

57. The apparatus of claim 49 wherein said computer system is comprised in a computer network.

58. The apparatus of claim 49 wherein said computer system comprises a neural network.

59. The apparatus of any of claim 49 wherein said computer system compares said received acoustic signal to a database containing information of one or more acoustic signals from said ossification-actuated skeletal structure to provide an estimate of bone age.

60. The apparatus of claim 49 wherein said computer system compares said received acoustic signal to a database containing information of one or more acoustic signals from said ossification-actuated skeletal structure to predict stature.

61. The apparatus of claim 49 wherein said computer system compares said received acoustic signal to a database containing information of one or more acoustic signals from said ossification-actuated skeletal structure to indicate, track or follow treatment of one or more of: a bone-growth related disorder, a growth plate disorder, and a growth related disorder.

62. A method for measuring bone age comprising:

transmitting acoustic energy into a region of the body of a subject at which cartilage of a skeletal structure is undergoing ossification or at which cartilage of a skeletal structure that has completed growth was last to ossify so that the acoustic energy propagates substantially transverse to the structure;

receiving an acoustic signal from the skeletal structure responsive to said transmitted acoustic energy;

analyzing the acoustic signal to determine at least one effect of said structure on said signal; and

estimating the age of the structure from said determined effect.

63. A method of determining bone age comprising:
measuring a first acoustic velocity through a bone in a direction transverse to the bone;
measuring a second acoustic velocity along a length of the bone;
determining a ratio between the first and second acoustic velocities; and
using the ratio to determine bone age.

(c)(1) (ix) Evidence Appendix: None

(c)(1) (x) Related Proceedings Appendix: None